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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,674	ALA'ALDEEN ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *1-66,68,70 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *080901*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 01/10/01, 12/02/02 and 11/05/03.

Election

2) Acknowledgment is made of Applicants' election, with traverse, filed 11/05/03, in response to the written lack of unity mailed 08/05/03. Applicants have elected invention VII, claims 67 and a part claim 69, drawn to SEQ ID NO: 2. Applicants' traversal is on the grounds that the concurrent examination of inventions VII and VIII will not place an undue burden on the Office, because the field of search for these groups should be substantially the same. Applicants contend that the subject matter of inventions VII and VIII overlap and that a search of class 424, subclass 249.1 is required for showings of *Neisseria*. Applicants cite MPEP § 803.04 and § 1850, and state that where there is no independent and distinct invention, up to ten sequences will be examined in one application. Applicants admit that the featured sequences of inventions VII and VIII are different, yet submit that claims of inventions VII and VIII do not cover independent and distinct inventions. Applicants further argue that inventions V and VI should also be examined in the present application, since these claims are directed to either nucleotide sequences or to the use of the claimed sequences for a medicament.

Applicants' arguments have been carefully considered, but are non-persuasive. As set forth in the written lack of unity mailed 08/05/03, the special technical features of inventions V and VI are DNA constructs comprising SEQ ID NO: 3 and SEQ ID NO: 1 or an active derivative thereof, respectively. The special technical features of inventions VII and VIII are vaccines comprising SEQ ID NO: 2 and SEQ ID NO: 4 respectively, and a method of using the same. The different inventions are not so linked as to form a single general inventive concept as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject matter of the different recognized inventions. The polynucleotides and the polypeptides do not share significant structural elements and/or immunogenic specificity and in addition belong to two distinct classes. Therefore, no claims drawn to polynucleotides, let alone ten polynucleotides would be joined with the elected polypeptide claims.

As readily acknowledged by Applicants, the two polypeptide, SEQ ID NO: 2 and SEQ ID NO: 4, do not share the same structure and therefore require separate structural or sequence searches. One search of class 424, subclass 249.1 would not yield prior art on two polypeptides having two separate structures or SEQ ID numbers. The methods of inventions I, II, III and IV do not share common method steps and/or reagents. Furthermore, the DNA molecules of inventions V and VI are not required for the methods of inventions I through IV. Additionally, the concept of using neisserial proteins or fragments thereof to induce an immune response in human T-cells was known in the prior art. For instance, Wiertz *et al.* (*Infect. Immun.* 64: 298-304, January 1996 - already of record). As is evident from the art rejection(s) made below, the special technical feature of invention VII, i.e., some of SEQ ID NO: 2 or an active derivative thereof, was already disclosed in the prior art, for instance, by Seid *et al.* (see below). Applicants should note that technically, this absence of special technical feature permits the separation of the methods of using the product from the product itself. Yet, the method of use as claimed via claim 69 has not been separated from invention VII and has been examined along with the product. For the reasons delineated above, the lack of unity held in the instant application is proper and is hereby made FINAL.

Status of Claims

3) Claims 3-5 and 57 have been amended via the amendment filed 01/10/01.

Claims 72-79 have been canceled via the amendment filed 01/10/01.

Claim 59 has been amended via the amendment filed 11/05/03.

Although the elected claims 67 and 69 are indicated as '(Original)', these claims in fact are amended claims, amended via the papers filed 11/05/03, and are non-identical to the original claims filed 01/10/01.

Claims 1-71 are pending.

Claims 1-66, 68, 70 and 71 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Elected claims 67 and 69, to the extent these claims encompass SEQ ID NO: 2, are under examination. A First Action on the Merits is issued for these claims.

Information Disclosure Statement

4) Acknowledgment is made Applicants' Information Disclosure Statement filed 08/09/01. The

information referred to therein has been considered and a signed copy is attached to this Office Action.

Sequence Listing

5) Acknowledgment is made of Applicants' submission of CRF and the raw Sequence Listing which have been entered 07/30/02.

Priority

6) The instant application is a national stage 371 application of PCT/GB99/02205, filed 07/09/1999 and claims priority to the foreign application, 9814902.4, filed 07/10/1998 in the United Kingdom.

It is noted that a certified copy of the priority document has been submitted to the Office.

Specification - Informalities

7) The instant specification is objected to because:

(i) The first paragraph of the specification does not accurately reflect the status of the prior application, as indicated above in italicized letters under 'Priority'.

(ii) The instant specification is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code, which Applicants are required to delete. For example, see line 3 on page 13. See MPEP § 608.01.

(iii) The use of the trademarks in the instant specification has been noted in this application. For example, see page 10 of the specification: 'Histopaque'. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(iv) Instant specification recites several citations of published references, which lack complete information with regard to the name of the journal or book, volume and/or page numbers. For example, see references cited on page 10, first full paragraph of the specification: 'Ala'Aldeen, 1994'; 'Sinigaglia, 1991' and 'Valitute, 1995' on page 11, first full paragraph; and 'Palmer, 1993' on page 14 under section 1. For clarity and completeness, it is suggested that Applicants amend the specification to provide the complete information for each of the publication cited in the text of the

instant specification.

(v) The instant application is informal in the format or arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the Applicants' use.

Content of Specification

(a) Title of the Invention: See 37 C.F.R 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.

(b) Cross-References to Related Applications: See 37 C.F.R 1.78 and M.P.E.P § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See M.P.E.P § 310.

(d) Reference to a "Microfiche Appendix": See 37 C.F.R 1.96(c) and M.P.E.P § 608.05. The total number of microfiche and the total number frames should be specified.

(e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 C.F.R 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms

the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 C.F.R 1.74. The recitation 'Figure Legends' on page 9 of the specification should be replaced with --Brief Description of the Drawings'--.

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 C.F.R 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 C.F.R 1.75 and M.P.E.P § 608.01(m). The claim or claims must commence on separate sheet. (37 C.F.R 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 C.F.R 1.81, 1.83-1.85, and M.P.E.P § 608.02.

(l) Sequence Listing: See 37 C.F.R 1.821-1.825.

Rejection(s) under 35 U.S.C. § 101

8) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

9) Claim 67 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claim 67, as written, does not sufficiently distinguish over a polypeptide, a fragment or a derivative thereof as it exists naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring product. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. The claim(s) should be amended to indicate the hand of the inventor, e.g., by insertion of a limitation, such as, 'Isolated" or "Purified" or "Isolated and purified" as the case may be in the instant specification. See MPEP 2105.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

10) Claims 67 and 69 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The recitation 'derivatives thereof' and/or 'some .... of the amino acid sequence as shown in SEQ ID NO: 2' (i.e., fragments) in the instant claims do not exist independent of their function(s), i.e., vaccine functions, or induction of specific T-cell proliferation, and prophylactic/therapeutic activity against neisserial disease. The specification discloses prophylactic or therapeutic applications/intentions for the claimed 'derivatives' or fragments. However, the instant specification fails to teach a single derivative or fragment of the polypeptide of SEQ ID NO: 2 having the above-cited functional activities. Prophylactic or therapeutic applications minimally require a specific proliferative action of the derivatives or fragments. The precise structure or relevant identifying characteristics of each 'derivative' or 'some of the amino acid sequence of SEQ ID NO: 2' having the

above-cited functional activities can only be determined empirically by actually making every DNA molecule that encodes the 'derivative' or fragment, and testing each DNA molecule to determine whether it encodes the 'derivative' or fragment having the particularly disclosed biological activities. The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

A mere statement in the specification that the invention includes the use of such a 'derivative' or fragment as a prophylactic or therapeutic product is insufficient to meet the adequate written description requirement of the claimed invention. The claimed molecule has specific functional or biologic properties dictated by the structure of the polypeptide and the corresponding structure of the gene sequence which encodes it. A convincing structure-function relationship has to exist between the structure of the gene sequence, the structure of the polypeptide derivative or fragment encoded, and the function of the encoded derivative or fragment. The function cannot be predicted from the modification of the structure of the gene and in the instant case, the DNA encoding the 'derivative' or 'fragment' of the polypeptide of SEQ ID NO: 2. Applicants have not shown that derivatization of a reference gene sequence encoding a reference polypeptide of SEQ ID NO: 2 as claimed would automatically predict the production of a 'derivative' or fragment having the recited functional activities. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of DNA molecules encoding a representative number of species of 'derivatives' or fragments of SEQ ID NO: 2 as recited, sufficient to allow one skilled in the art to determine that the inventors had possession of the invention as claimed. With the exception of a polypeptide having the specific amino acid sequence of SEQ ID NO: 2, a skilled artisan cannot envision the detailed chemical structure of all the 'derivative' or fragment species encompassed by the recited molecule. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. The 'derivatives' or 'some of the amino acid sequence' of SEQ ID NO: 2, or the DNAs encoding the same themselves are required. See *Fiers v. Revel, 25 USPQ2d*

1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.*

11) Claims 67 and 69 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a composition comprising a T cell-stimulating meningococcal polypeptide having the amino acid sequence of SEQ ID NO. 2, does not reasonably provide enablement for a 'vaccine' comprising the same or an 'active derivative thereof' and for a method of treatment of any neisserial disease comprising induction of T-cell proliferation with the polypeptide having SEQ ID NO. 2 or 'active derivatives thereof', as claimed in a broad sense. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention commensurate in scope with these claims.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the specification is enabling for a T cell-stimulating meningococcal polypeptide comprising the amino acid sequence of SEQ ID NO: 2. However, a 'vaccine' comprising the polypeptide of the amino acid sequence, SEQ ID NO: 2, or an active derivative thereof against the generically recited 'neisserial disease', and a method of treatment of such a disease with the polypeptide of the amino acid sequence, SEQ ID NO: 2 or active derivative(s) thereof as recited, are not enabled. How to practice the method of claim 69 is not described. What steps should be followed, *in vivo* or *in vitro*, in the claimed method, and whether or not one should administer the polypeptide of the amino acid sequence, SEQ ID NO: 2, or an active derivative thereof, and, if so, to whom or which species or subjects is not described. The generic term 'neisserial disease' is so broad that it encompasses a myriad of clinical conditions caused by *Neisseria*, such as, systemic or local meningococcal infections, including septicaemia, pneumonia, meningitis etc., and a variety of gonococcal infections including sexually transmitted diseases,

urethritis, cervicitis, proctitis, pharyngitis, salpingitis, epididymitis and bacteremia/arthritis etc. The limitation 'some .. of the amino acid sequence as shown in SEQ ID NO: 2 or an active derivative thereof' encompasses an infinite number of molecules, including all types of the polypeptide variants having amino acid substitutions, deletions, and insertions; and polypeptide fragments of varying length, structure and size. It should be noted that the term 'vaccine' by definition is required to induce 'protective antibodies' against any neisserial species that causes a disease, including known neisserial pathogenic species, those yet to be discovered and those whose pathogenetic nature or mechanism is yet to be established. The species of the pathogenic *Neisseria* that cause the disease are not identified and the nature of their pathogenesis is not described. Without the disclosure of the precise pathogenesis caused by a representative number of these currently undisclosed strains of unspecified species of pathogenic *Neisseria* and without the establishment, via an art-accepted *in vivo* animal model, or an *in vitro* assay that is correlative of protection showing that the claimed 'vaccine' elicits protective antibodies against all these unspecified strains and unspecified species of pathogenic *Neisseria*, one of skill in the art would not be able to practice the invention as claimed without considerable amount of undue experimentation. Infection due to *Neisseria meningitidis* or *Neisseria gonorrhoea* encompasses microbial cell invasion and growth or multiplication of the bacteria. The specification is not supportive of a vaccine which keeps the process of meningitis, septicaemia, pneumonia or other manifestations of systemic or local disease occasioned by *Neisseria meningitidis* from happening, or the process of sexually transmitted diseases, urethritis, cervicitis, proctitis, pharyngitis, salpingitis, epididymitis and bacteremia/arthritis etc. due to *Neisseria gonorrhoea* from happening, or a vaccine which prevents the entry/invasion of *Neisseria meningitidis* or *Neisseria gonorrhoea* into a cell or its internal dwelling by induction of T cell proliferation with the polypeptide or an active derivative thereof of the instant invention. There is absolutely no evidence within the instant specification to show that the vaccine as claimed was in fact therapeutic against a single neisserial disease caused by a single species of a single pathogenic member of the genus *Neisseria*. There is no showing that the claimed polypeptide, some part of it, or its active derivative is produced by any and every pathogenic *Neisseria* such that it induces protective or therapeutic effects. The specification fails to teach that the T-cell proliferative response induced by the meningococcal polypeptide of SEQ ID NO: 2, or a fragment or derivative thereof, is

immunologically cross-protective against infection by any isolate or species of any *Neisseria*, as claimed currently. In fact, the specification at fifth paragraph on page 13 states that the exact polypeptide sequence can vary among different isolates of meningococci. Thus, the ability to reproducibly practice the claimed invention is well outside the realm of routine experimentation.

Vaccines are required to elicit an immunoprotective response in the vaccinated host. While induction of an immune response in a host by a bacterial or meningococcal polypeptide antigen is generally predictable, induction of a protective immune response by such a polypeptide antigen, a derivative or a fragment thereof against homologous and heterologous meningococcal or neisserial strains, serogroups or subtypes is not a predictable event. Other than a showing in the instant specification that the meningococcal polypeptide of SEQ ID NO: 2 has T cell-stimulating properties, there is no evidence within the instant specification that the polypeptide of SEQ ID NO: 2, its fragments, variants or derivatives serve as 'vaccines' against any neisserial disease, or are effective in a method of treatment of any neisserial disease by induction of T cell proliferation. The art of vaccines recognizes the unpredictability associated with whether an antigen or immunogenic component derived from a microbial pathogen is immunoprotective. For instance, Ellis RW (*Vaccines*, (Eds) Plotkin *et al.*, W.B. Saunders Company, Philadelphia, Chapter 29, 1988, see page 571, second full paragraph) reflects this problem in the teaching that the key to the problem of vaccine development "is the identification of that protein component of a ..... microbial pathogen that itself can elicit the production of protective antibodies ..... and thus protect the host against attack by the pathogen". In the instant case, the specification fails to teach or show that the isolated polypeptide of the amino acid sequence SEQ ID NO: 2, a part of the sequence, or an active derivative thereof, alone or in combination with other antigens, does in fact induce an immune response or a T-cell proliferative response that is protective against the homologous or heterologous strain or species of *Neisseria*. The selection of an immunogenic component that is protective from a myriad of immunogenic components present on the microbial surface, or produced by a microbial pathogen cannot be accomplished with a predictable precision, without undue experimentation. The specification fails to teach that the mere presence of T cells induced with the polypeptide of SEQ ID NO: 2, a fragment, or a derivative thereof provides protection from infection by any isolate or species of the genus *Neisseria*. There is no evidence within the instant specification that the claimed

polypeptide, a fragment, or a derivative thereof is able to perform as a vaccine by conferring protection, or eliminating the disease, or lowering the morbidity and/or mortality of any neisserial disease caused by an isolate or species of the genus *Neisseria*.

Absent a showing that the isolated or the non-isolated polypeptide of SEQ ID NO: 2, a fragment, or a derivative thereof, is effective in inducing a 'protective' T-cell proliferation against homologous infection by an isolate of *Neisseria*, or against a heterologous infection by a heterologous species of *Neisseria*, the vaccine composition and the method of treatment as claimed are not enabled. In view of the lack of specific guidance and teachings and the lack of enabling disclosure within the instant specification, the lack of working examples enabling the full scope of the claims, the breadth of the claims, the protective unpredictability recognized in the art, and the quantity of the experimentation required, undue experimentation would have been required by one of ordinary skill in the art to reproducibly practice the full scope of the invention, as claimed. The instant claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

12) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

13) Claims 67 and 69 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 67 and 69 are vague and indefinite in the recitation 'active derivative thereof' or 'active derivative(s) thereof', because it is unclear what is encompassed in this limitation. What constitutes a derivative, and how much of the polypeptide's original structure has to be retained such that the resulting product can be considered as a 'derivative', is not clear. What activity should a polypeptide have in order to qualify as an 'active derivative' is unclear. The metes and bounds of the structure encompassed in the limitation 'active derivative' is indeterminate.

(b) Claim 67 is vague and/or incorrect in lacking a preceding article in between the limitations: 'against neisserial disease' and 'comprising polypeptide'. For clarity, it is suggested that

Applicants replace the limitations with --against a neisserial disease-- and --comprising a polypeptide-- respectively.

(c) Claim 69 is vague and/or incorrect in lacking a preceding article in between the limitations: 'of neisserial disease' and 'with polypeptide'. For clarity, it is suggested that Applicants replace the limitations with --against of a neisserial disease-- and --with a polypeptide-- respectively.

(d) Claim 69 does not recite positive active steps so that the claim sets out and circumscribe particular areas with reasonable degree of precision and particularity and make clear what subject matter the claims encompass, as well as make clear the subject matter from which others would be precluded. See *Ex parte Erlich, 3 USPQ2d 1011 (BPAI, 1987)*. Claim is incomplete because it omits essential steps. There are no steps delineating the claimed method of treatment. What *in vivo* or *in vitro* step is involved in inducing T-cell proliferation with the polypeptide is not clear. Whether or not the claimed method includes *in vivo* administration of the polypeptide to a subject is not clear.

Rejection(s) under 35 U.S.C § 102

14) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15) Claims 67 and 69 are rejected under 35 U.S.C § 102(b) as being anticipated by Seid *et al.* (WO 90/06696).

Seid *et al.* disclosed a vaccine effective against a neisserial disease, i.e., meningococcal disease, comprising a polypeptide, a fragment or an oligopeptide thereof having some of the amino acid sequence of, or an active derivative of the instantly recited SEQ ID NO: 2. Seid's polypeptide comprises the T cell epitopic peptide GLAG which is the same peptide present at positions 578 to 581 of the instantly recited SEQ ID NO: 2. See abstract; claims; and Table 7 of Seid *et al.* Seid's GLAG peptide constitutes some of the amino acid sequence of the instantly recited SEQ ID NO: 2, or as an active derivative of SEQ ID NO: 2. Seid *et al.* also disclosed a method of eliciting a protective immune response (i.e., a method of treatment) against *Neisseria meningitidis* comprising

administering the vaccine that contains the T cell epitope (see claims 28-37). Seid's method induced T-cell proliferation (see Example 16).

Claims 67 and 69 are anticipated by Seid *et al.*

Objection(s)

16) Claims 67 and 69 are objected to for the following reasons:

(a) Claim 69 is objected to for including non-elected subject matter.

(b) Claims 67 and 69 are objected to for the incorrect recitation 'SEQIDNO2' as opposed to --SEQ ID NO: 2--.

Remarks

17) Claims 67 and 69 stand rejected.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives papers 24 hours a day and seven days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347 or (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909 or (571) 272-0864.

January, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER